

Recurrent Pregnancy Loss

Definition

A pregnancy loss or miscarriage is the spontaneous loss of a pregnancy before 24 weeks of gestation while the loss of a pregnancy after 24 weeks of gestation is called a stillbirth.

Early miscarriages (less than 3 months of pregnancy) are common, with 10-20 in 100 (10-20%) pregnancies ending this way. Late miscarriages, after 3 months of pregnancy but before 24 weeks, are less common: 1-2 in 100 (1-2%) pregnancies end in a late miscarriage.

Recurrent Pregnancy Loss or Recurrent Miscarriage is defined as three or more consecutive pregnancy losses, without a baby in between losses.. Ectopic pregnancies and molar pregnancies are not included. Recurrent pregnancy loss affects 1-2% (1-2 women out of 100) of couples. This recurring loss is often very distressing for couples, especially as there is still a limited understanding of the problem. In most cases, the cause is not apparent and can involve detailed investigations.

Investigations to try and determine the cause may be considered in older (over 37 years) or particularly anxious women after 2 miscarriages.

It is important for couples to understand that recurrent miscarriage is a specialist area and tests need to be undertaken and interpreted with expert medical guidance. The information below is to help couples have a better understanding of their situation, after consultation with specialists.

You may request to be referred to a specialist recurrent pregnancy loss (Recurrent Miscarriage) clinic, especially if you are older or have a complex medical history.

The causes of recurrent miscarriage along with the recommended investigations are discussed below. The list is by no means exhaustive.

Unexplained Recurrent Pregnancy Loss

This accounts for most of the cases. It is a diagnosis by exclusion, meaning all tests undertaken return as normal so it is assumed the cause is idiopathic or unexplained. Foetal heart activity is almost never seen, and loss usually occurs before 8 weeks. Foetal chromosomal anomalies occur in about 50% of sporadic and possibly recurrent pregnancy loss, usually in those over 37 years of age and at less than 10weeks of gestation.

The two main predictive factors for a future successful pregnancy are maternal age and the

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number of previous losses. For example, at age 30, there is an 80% chance of a future successful pregnancy even after 3 miscarriages and a 71% chance after 5 miscarriages. At age 40, this drops to 64% and 52% after 3 and 5 losses respectively.

Treatment: Early pregnancy assessment, using `tender loving care` (TLC), and regular scans provides adequate support, providing reassurance to anxious women, who will usually go on to have a successful pregnancy. Hormone treatment or immunological therapy are recommended only under specialist guidance in individualised situations, as generally not shown to improve pregnancy outcome.

Nutrition/Environmental factors

Excessive consumption of coffee, smoking, alcohol and selenium deficiency has all been associated with spontaneous pregnancy loss. There is no safe limit for alcohol even when not pregnant.

Avoid hard and soft drugs.

Being overweight or obese increases the risk of pregnancy loss. Underlying factors such as Polycystic Ovarian Syndrome (PCOS See leaflet) should be identified and managed appropriately.

Following a mostly whole food plant based way of eating can help sustainable weight loss. The diet should predominantly consist of vegetables, intact whole grains, fruits, beans, legumes, herbs and spices and some nuts and seeds with water as the drink of choice. Avoid refined foods including junk and ultraprocessed foods, oils, alcohol and foods of animal origin. *See nutrition leaflet.*

Consider taking Vitamin D supplements after having your levels checked.

Maternal diseases such as diabetes and thyroid disorders (including thyroid antibodies) may have an increased risk for recurrent loss and once treated satisfactorily should be not responsible for recurrent pregnancy loss.

Oligomenorrhoea

Women with cycle lengths of >35 days regularly are at higher risk of recurrent pregnancy loss (usually 6-8 weeks, foetal heart never seen). This is seen in 10-15% of women with recurring miscarriage compared to 1% of general population. The miscarriage is usually of

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normal karyotype. HCG hormone therapy for this group may improve pregnancy outcome. Specialised individual management is recommended.

Antiphospholipid syndrome (APS)

With APS (a syndrome that makes your blood more likely to clot), pregnancy loss often occurs after 10 weeks of gestation. Foetal heart activity is often seen and then lost on scans, unlike in idiopathic cases where it is rarely seen.

APS may be responsible for up to 30% of cases in women with mid trimester loss (after 14 weeks gestation) but may be seen with first trimester loss (15%).

10% of women with mid trimester loss may have more than one cause. To fulfil diagnostic criteria, the patient should have:

At least one of the following clinical features:

- Recurrent (three or more) pregnancy loss
- Intrauterine foetal loss in second or third trimester
- Pre-eclampsia
- Intrauterine growth restriction

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Abnormal result of one of the following blood tests on more than one occasion (2 separate measurements, at least 6 weeks apart)

- Prolonged DRVTT (dilute Russell viper venom test) for lupus anticoagulant (LAC)
- IgG or IgM anticardiolipin antibody (ACA)

Women with recurrent pregnancy loss and positive APS should be managed by specialists, ideally in a recurrent pregnancy loss clinic. Low dose aspirin is often used in the pregnancy. Low molecular weight heparin or similar medications may be added, especially, if there is history of maternal thrombosis. Postnatal thromboprophylaxis for 6 weeks, if there are other risks factors should be considered.

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Thrombophilias

Thrombophilias such as Protein C and S deficiency, activated protein C resistance (APCR)-Factor V Leiden mutation should be tested for in women with recurrent pregnancy loss. Thrombophilia is an inherited condition that means that your blood may be more likely to clot and may cause recurrent pregnancy loss and especially late pregnancy loss.

Bacterial vaginosis

Polymicrobial infection may be responsible for 5-10% of mid trimester losses. This infection may also be associated with preterm labour and premature rupture of membranes. Other infections (TORCH, Chlamydia) are usually non-recurrent - so there is no need for routine repeated checks.

Uterine abnormalities

Uterine abnormalities, changing the normal shape of the uterine(womb) cavity account for less than 5% of mid trimester losses. Uterine septum can be a thin or thick band and is usually the commonest type of uterine abnormality.

A camera test (Hysteroscopy) or a specialised pelvic ultrasound scan (Hycosy) may be preferred over a dye test to outline the womb cavity and fallopian tubes (HSG: hysterosalpingogram) to detect septae, adhesions (scar tissue), cervical (neck of the womb) length and cervical patency.

At hysteroscopy (see leaflet), treatment may be carried out at the same time and a laparoscopic (keyhole) guided hysteroscopic resection may be needed in certain cases.

Cervical incompetence

Cervical incompetence (weakness of the neck of the womb contributing to pregnancy loss) can often be difficult to diagnose. A weak neck of the womb may occur in women without a specific reason or it may follow as a result of treatment to the cervix (for example knife cone biopsy and sometimes after a LLETZ procedure to treat precancerous cells on the cervix (see LLETZ leaflet). A weak neck of the womb may be inherited in certain of musculoskeletal disorders and may also occur after a traumatic vaginal delivery or termination.

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It is important to request your detailed medical notes as this can help your specialist to help you make fully informed decisions regarding the management of your case.

A careful clinical history and a pelvic ultrasound scan measuring cervical length, cervical patency and cervical assessment is needed before deciding on a cervical cerclage (Cervical stitch).

Parental chromosomal anomalies

Occur in about 4% of couples compared with 0.2% in the normal population. Balanced translocation is the most common of all chromosomal abnormalities. Genetic counselling and checking family members may be advised, depending on individual cases.

Sperm DNA fragmentation

There is now some evidence that damaged sperm could increase the risk of pregnancy loss and assessing sperm DNA damage could be considered in couples with specialist input in individualised situations.

Immune factors

May play a role in some women who miscarry repeatedly. This is known as an alloimmune reaction. Further research is needed in this area as not enough is known and any investigation or treatment should be only offered in a highly specialised setting.

The following links may be of further help

https://www.eshre.eu/-/media/sitecore-files/Guidelines/Recurrent-pregnancy-loss/ESHRE-RP L-patient-Guideline_22012018.pdf?la=en&hash=1E6C2A2DDF38FB6859A6CAFE449D4B648CC5811C

<https://www.rcog.org.uk/globalassets/documents/patients/patient-information-leaflets/pregnancy/pi-recurrent-and-late-miscarriage—tests-and-treatment-of-couples.pdf>

www.miscarriageassociation.org.uk

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